

WE CLAIM:

1. An isolated polypeptide comprising a truncated tryptophanyl-tRNA synthetase polypeptide comprising a Rossmann fold nucleotide binding domain, wherein the isolated polypeptide is capable of regulating vascular endothelial cell function.
2. The isolated polypeptide of claim 1, wherein the truncated polypeptide has a size of at least about 46 kilodaltons.
3. The isolated polypeptide of claim 1, wherein the truncated tRNA synthetase polypeptide has amino-terminal truncation.
4. The isolated polypeptide of claim 1, wherein the polypeptide is angiogenic.
5. The isolated polypeptide of claim 1, wherein the polypeptide is angiostatic.
6. The isolated polypeptide of claim 1, wherein the truncated tRNA synthetase polypeptide is a member of the group consisting of
 - a polypeptide consisting essentially of amino acid residues 48-471 of SEQ ID NO:9;
 - a polypeptide consisting essentially of amino acid residues 71-471 of SEQ ID NO:9;
 - a polypeptide of approximately 47 kD molecular weight produced by cleavage of the polypeptide of SEQ ID NO:9 with polymorphonuclear leucocyte elastase; and
 - fragments thereof comprising the amino acid sequence
-Asp-Leu-Thr-.
7. The isolated polypeptide of claim 1, wherein the polypeptide is mammalian.
8. The isolated polypeptide of claim 1, wherein the polypeptide is human.
9. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polynucleotide of SEQ ID NO:9;

(b) a polynucleotide which is hybridizable to a polynucleotide of SEQ ID NO:9;

(c) a polynucleotide encoding a polypeptide of claim 1;

5 (d) a polynucleotide that is hybridizable to a polynucleotide encoding a polypeptide of claim 1;

(e) a polynucleotide encoding a polypeptide of claim 6;

(f) a polynucleotide that is hybridizable to a polynucleotide encoding a polypeptide of claim 6;

10 (g) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:9; and

(h) a polynucleotide that is hybridizable to a polynucleotide encoding a polypeptide epitope of SEQ ID NO:9.

15 10. An isolated nucleic acid molecule of SEQ ID NO:9, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the 5'-terminus or the 3'-terminus.

11. A recombinant vector comprising an isolated nucleic acid molecule of SEQ ID NO:9.

20 12. A method of making a recombinant host cell comprising introducing an isolated nucleic acid molecule of SEQ ID NO:9 into the host cell.

13. A recombinant host cell produced by the method of claim 12.

14. The recombinant host cell of claim 13 comprising a vector sequence that includes a nuclear acid molecule of SEQ ID NO:9.

25 15. An isolated antibody that binds specifically to an isolated polypeptide of claim 1.

16. A recombinant host cell that expresses an isolated polypeptide of claim 1.

17. A method of making an isolated polypeptide comprising:

30 (a) culturing the recombinant host cell of claim 16 in which said polypeptide is expressed; and

(b) isolating expressed polypeptide from the cell culture.

18. A process for producing the polypeptide of claim 1, comprising treating tryptophanyl-tRNA synthetase with a protease.

19. The process of claim 18, wherein the protease is polymorphonuclear leukocyte elastase.

5 20. An isolated polypeptide which is a truncated mammalian tryptophanyl-tRNA synthetase polypeptide having chemokine activity.

21. The isolated polypeptide of claim 20, wherein the truncated polypeptide has an amino-terminal truncation.

10 22. The isolated polypeptide of claim 20, wherein the polypeptide has angiogenic activity.

23. The isolated polypeptide of claim 22, wherein the angiogenic activity is at least two-fold greater than control levels.

24. The isolated polypeptide of claim 20, wherein the polypeptide has angiostatic activity.

15 25. The isolated polypeptide having angiostatic activity of claim 24, wherein the polypeptide suppresses at least ten percent of angiogenic activity.

26. The isolated polypeptide having angiostatic activity of claim 24, wherein the polypeptide suppresses at least ninety percent of angiogenic activity.

20 27. An isolated nucleic acid molecule that encodes the polypeptide of claim 20.

28. A recombinant vector comprising the isolated nucleic acid molecule of claim 27.

25 29. A recombinant host cell comprising the isolated nucleic acid molecule of claim 27.

30 30. An isolated antibody that binds specifically to the isolated polypeptide of claim 20.

31. A recombinant host cell that expresses the isolated polypeptide of claim 20.

30 32. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 31 in which said polypeptide is expressed; and

(b) isolating expressed polypeptide from the cell culture.

33. A process for producing the polypeptide of claim 20, comprising treating tryptophanyl-tRNA synthetase with a protease.

5 34. The use of the isolated polypeptide of claim 1 for the preparation of a pharmaceutical composition for transdermal, transmucosal, enteral or parenteral administration.

10 35. A method of preparing a pharmaceutical composition suitable for transdermal, transmucosal, enteral or parenteral administration comprising the step of combining the isolated polypeptide of claim 1 and a pharmaceutically suitable excipient.

36. A composition comprising the isolated polypeptide of claim 1 and a pharmaceutically suitable excipient.

37. A composition comprising the isolated polypeptide of claim 6 and a pharmaceutically suitable excipient.

15 38. A composition comprising the isolated polypeptide of claim 20 and a pharmaceutically suitable excipient.

39. A method of suppressing angiogenesis in a mammal comprising the step of administering to the mammal an angiostatically effective amount of the composition of claim 37.

20 40. The method of claim 39, wherein the mammal is a human.

41. A method of treating, in a mammal, a condition that would benefit from decreased angiogenesis comprising the step of administering to the mammal an angiostatically effective amount of the composition of claim 37.

42. The method of claim 41, wherein the mammal is a human.

25 43. A method of treating a solid tumor in a mammal comprising the step of administering an angiostatically to the mammal effective amount of the composition of claim 37.

44. The method of claim 43, wherein the mammal is a human.

30 45. A method of suppressing tumor metastasis in a mammal comprising the step of administering an angiostatically effective amount of the composition of claim 37.

46. The method of claim 45, wherein the mammal is a human.

47. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 9; and

5 (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the determined presence or absence of said mutation.

48. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

10 (a) determining the presence or amount of expression of the polypeptide of claim 1 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the determined presence or amount of expression of the polypeptide.

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